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ELF ATOCHEM NORTH AMERICA, INC.
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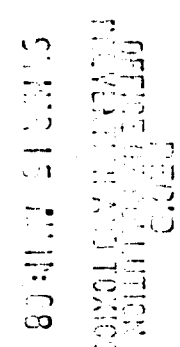
(A)

Contains No CBI

March 10, 1994

FEDERAL EXPRESS
RETURN RECEIPT REQUESTED



Document Processing Center (TS-790)
Office of Toxic Substances
Environmental Protection Agency
401 M St. S.W.
Washington, D.C. 20460
Attn: Section 8(e) Coordinator

Subject: TSCA Section 8(e) Submission

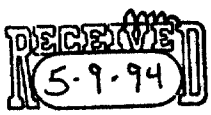
Dear Sir/Madam:

Elf Atochem North America Inc. is submitting the attached study to the Environmental Protection Agency (EPA) pursuant to Toxic Substances Control Act (TSCA) Section 8(e). This study provides information on Cyclohexyl Mercaptan (CAS No. 1569-69-3) and does not involve effects in humans. The title of the enclosed study report is Cyclohexyl Mercaptan Skin Sensitization Test in Guinea-Pigs (Maximization method of Magnusson, B. and Kligman, A.M.).

Nothing in this letter or the enclosed study report is considered confidential business information of Elf Atochem.

The following is a summary of the adverse effects observed in the skin sensitization test.

Cyclohexyl Mercaptan was tested for potential to produce allergic skin reaction by intradermal injection and skin application to guinea pigs using a modified Magnusson and Klingman method. After challenge application, the test material produced well-defined erythema in 20% (4/20) animals, and very slight erythema in 75% (15/20) animals and was classified as a weak sensitizer.



35 pgs.

Elf Atochem has not previously filed any 8(e) notices or Premanufacture Notifications (PMNs) on the subject material.

Results from the study report will be incorporated into the current Elf Atochem Material Safety Data Sheet for Cyclohexyl Mercaptan.

Further questions regarding this submission may be directed to me at (610) 337-6892.

Sincerely,

C.H. Farr, PhD, DABT
Manager, Product Safety
and Toxicology

Enclosure

SPONSOR

Elf Atochem Rotterdam B.V.
Postbus 6030
3196 XH Vondelingenplaat/Rt
The Netherlands

STUDY TITLE

SKIN SENSITIZATION TEST IN GUINEA-PIGS (Maximization method of Magnusson, B. and Kligman, A.M.)

TEST SUBSTANCE

CYCLOHEXYL MERCAPTAN

STUDY DIRECTOR

Jack Clouzeau

STUDY COMPLETION

20th January 1994

PERFORMING LABORATORY

Centre International de Toxicologie (C.I.T.)
Miserey - 27005 Evreux - France

LABORATORY STUDY NUMBER

10873 TSG

CONTENTS

STATEMENT OF THE STUDY DIRECTOR

This study was performed in accordance with the protocol agreed upon by Elf Atochem Rotterdam B.V., according to the maximization method of Magnusson and Kligman and according to:
. O.E.C.D. guideline No. 406, 12th May 1981.

The study was conducted in compliance with the principles of Good Laboratory Practice Regulations:
. O.E.C.D. Principles of Good Laboratory Practice, C(81)30(final) Annex 2. May 12, 1981.

I declare that this report constitutes a true and faithful record of the procedures undertaken and the results obtained in the performance of the study.

There were no influences, impacts or circumstances noted which might have impaired the integrity of this study.

This study was performed at the Centre International de Toxicologie (C.I.T.), Miserey, 27005 Evreux, France.

Toxicology

J. Clouzeau Date: 20.1.94
Biologist

OTHER SCIENTISTS INVOLVED IN THIS STUDY

Pharmacy

J. Richard
Doctor of Pharmacy

Toxicology

C. Pelcot
Study Supervisor

STATEMENT OF THE QUALITY ASSURANCE UNIT

The protocol, study (main) and report were inspected by the C.I.T. Quality Assurance Unit on the following dates:

Inspection	Date of inspection	Date of inspection report
Protocol	28.6.93	28.6.93
Test substance/preparation	1.10.93	1.10.93
Report (first typing)	23.12.93	23.12.93
Report (final)	20.1.94	20.1.94

The other stages (of the same type of studies) were inspected routinely on the following dates:

Animals/housing	14.10.93	14.10.93
Treatment	5.10.93	5.10.93

The inspections were performed in accordance with C.I.T. procedures and the principles of Good Laboratory Practice Regulations.

p/o

M. Labiche Date: 20.1.94
Pharmacist
Head of Quality Assurance Unit
and Scientific Archives

SUMMARY

At the request of Elf Atochem Rotterdam B.V., The Netherlands, the potential of the test substance, CYCLOHEXYL MERCAPTAN, to induce delayed contact hypersensitivity following intradermal injection and cutaneous application was evaluated in guinea-pigs according to the maximization method of Magnusson and Kligman and O.E.C.D. (No. 406, 12th May 1981). The study was conducted in compliance with the Principles of Good Laboratory Practice Regulations.

Methods

Thirty guinea-pigs (15 males and 15 females) were allocated to 2 groups: a control group 1 (5 males and 5 females) and a treated group 2 (10 males and 10 females).
The sensitization potential of the test substance was evaluated after a 10-day induction period during which time the animals were treated with the vehicle (control group) or the test substance (treated group). On day 1, in presence of Freund's complete adjuvant, 0.1 ml of the test substance at a concentration of 25% in the vehicle was administered by intradermal route. On day 8, 0.5 ml of the test substance in its original form was applied by cutaneous route during 48 hours by means of an occlusive dressing. After a period of 12 days without treatment, a challenge cutaneous application of 0.5 ml of the vehicle (left flank) and 0.5 ml of the test substance in its original form (right flank) were administered to all animals.
The test substance and the vehicle were prepared on a compress then were applied to the skin and held in place for 24 hours by means of an occlusive dressing. Cutaneous reactions on the challenge application sites were then evaluated 24 and 48 hours after removal of the dressing.

After the final scoring period, the animals were sacrificed and cutaneous samples were taken from the challenge application sites from all the animals. No histological examination was performed on the cutaneous samples.

The sensitivity of the guinea-pigs in C.I.T. experimental conditions were checked in a recent study with a positive sensitizer: Dinitro 2.4 Chlorobenzene. During induction period the test substance was applied at 0.05% (day 1) and 0.5% (day 8) concentrations. At cutaneous challenge application, 0.1% and 0.5% were tested on both flanks.

Results

No clinical signs and no deaths were noted during the study.

Sensitization skin reactions characterised by a well-defined erythema (score of 2) were observed after 24 hours on the right flank of 4/20 treated animals. No cutaneous reactions were noted in 1 animal. Inconclusive evidence of sensitization skin reactions (very slight erythema, score of 1 after 24 and 48 hours) were noted in 9/20 treated animals. After 48 hours, erythema reversed in 6/20 animals. No oedema was observed.

The guinea-pigs which were used showed a satisfactory sensitization response in 100% animals using a positive sensitizer (appendix 5).

Conclusion

The test substance, CYCLOHEXYL MERCAPTAN, induced positive skin sensitization cutaneous reactions in 4/20 (20%) guinea-pigs. The allergenicity level of the test substance, CYCLOHEXYL MERCAPTAN, was WEAK (II) in guinea-pigs.

1. INTRODUCTION

The objective of this study, performed according to maximization method established by Magnusson and Kligman (1), was to evaluate the potential of the test substance, CYCLOHEXYL MERCAPTAN, to induce delayed contact hypersensitivity in guinea-pigs.

The results of the study are of value in predicting the contact sensitization potential of the test material in Man.

During the induction period, the test substance was administered by intradermal route (together with an adjuvant to maximise potential reactions) and cutaneous route. After a rest period of 12 days, a challenge application with the test substance was performed in order to provoke a cutaneous sensitization reaction.

The study was conducted in compliance with:
. O.E.C.D. guideline No. 406, 12th May 1981.

2. MATERIALS AND METHODS

2.1. TEST AND CONTROL SUBSTANCES

2.1.1 Test substance

The test substance, CYCLOHEXYL MERCAPTAN, used in the study was supplied by Elf Atochem Rotterdam B.V.

Documentation supplied by the Sponsor identified the test substance as follows:
. protocol:
  - denomination: CYCLOHEXYL MERCAPTAN
  - batch No.: 93-6171
. labelling:
  - denomination: CYCLOHEXYL MERCAPTAN; N° d'archivage au CAL: 3416/93
  - batch number: 93-6171
. description:colourless liquid
. container: a metallic box containing a glass flask
. date of receipt: 13.7.93
. storage conditions: room temperature, protected from light
. purity: 99.6%

Data relating to the characterization of the test substance are documented in a test article description and a certificate of analysis (presented in appendix 1) provided by the Sponsor.

2.1.2 Vehicle

The vehicle used was paraffin oil, batch No. 4547 (Coopérative Pharmaceutique Française, 77000 Melun, France).

(1) Magnusson, B.; Kligman, A.M.: The identification of contact allergens by animal assay. The guinea-pig maximization test. J. Invest. Derm. 52: 268-276 (1969).

2.1.3 Other substances

The other substances used were:
. sterile isotonic aqueous NaCl solution, batch No. 3019 (Biosédra, 92240 Malakoff, France);
. Freund's complete adjuvant, batch No. 29829 (Osi, 75739 Paris, France);
. sodium laurylsulphate, batch No. 112H0485 (Aldrich, 67000 Strasbourg, France);
. vaseline, batch No. 3006 (Monot, 21801 Quétigny, France).

2.2. TEST SYSTEM

2.2.1 Animals

Species and strain: Dunkin-Hartley guinea-pigs.
Reason for this choice: species recommended by the international regulations for sensitization studies. The strain used has been shown to produce a satisfactory sensitization response using known positive sensitisers.
Breeder: Centre d'Elevage Lebeau, 78950 Gambais, France.
Number: 30 animals (15 males and 15 females).
Allocation of the animals to the groups: on day -1, the animals were weighed and randomly allocated to 2 groups: a control group 1 consisting of 10 animals (5 males and 5 females) and a treated group 2 consisting of 20 animals (10 males and 10 females).
Weight: on day 1, the animals had a mean body weight of 425 ± 23 g for the males and 412 ± 25 g for the females.
Acclimatization: at least 5 days before the beginning of the study.
Identification of the animals: the animals were identified individually by an ear-tattoo.

2.2.2 Environmental conditions

During the acclimatization period and throughout the study, the conditions in the animal room were as follows:
. temperature: 22 ± 3°C
. relative humidity: 50 ± 20%
. light/dark cycle: 12 h/12 h
The air was non-recycled and filtered.
During the acclimatization period and throughout the study, the animals were housed individually in polycarbonate cages (48 x 27 x 20 cm) equipped with a polypropylene bottle. Sifted and dusted sawdust was provided as litter (SICSA, 92142 Alfortville, France). An analysis of potential residues and major contaminants is performed periodically (Laboratoire Wolff, 92110 Clichy, France).

2.2.3 Food and water

During the study, the animals had free access to "Guinea-pigs sustenance reference 106 diet" (U.A.R., 91360 Villemoisson-sur-Orge, France).
Food was periodically analysed (composition and contaminants) by the supplier.
The diet formula is presented in appendix 2.

Drinking water filtered by a F.G. Millipore membrane (0.22 micron) was contained in bottles.
Bacteriological and chemical analysis of the water and detection of possible contaminants (pesticides, heavy metals and nitrosamines) are performed periodically.
Results are archived at C.I.T.

There were no contaminants in the diet, water or sawdust at levels likely to have influenced the outcome of the study.

2.3. TREATMENT

2.3.1 Preliminary test

A preliminary test was performed to define the concentration to be tested in the main study.

By intradermal route

Determination of the Minimum Irritant Concentration (M.I.C.):

. 24 hours before treatment, the dorsal region of the animals was clipped,
. the test substance was prepared in an appropriate vehicle,
. intradermal administration of the test substance (volume 0.1 ml) at increasing concentrations was performed in order to determine the maximum concentration which does not cause necrosis or ulceration, but a slight irritation,
. evaluation of the potential cutaneous reactions, 24 and 48 hours after injection.

By cutaneous route

Determination of the Minimum Irritant Concentration (M.I.C.) and Maximum Non-Irritant Concentration (M.N.I.C.):

. 24 hours before treatment, the dorsal region of the animals was clipped,
. if necessary the test substance was suspended in an appropriate vehicle,
. 0.5 ml of each concentration was applied to a gauze patch of approximately 4 cm^2 and then held in place by an occlusive dressing for 24 hours (2 concentrations per animal),
. potential cutaneous reactions were evaluated 24 hours after removal of the gauze patches.

No residual test substance was observed upon removal of the dressings.

2.3.2 Main study

2.3.2.1 Preparation of the animals

For all animals and before each treatment, the application sites were:

. clipped on days -1 and 7 (scapular area 4 x 2 cm),
. clipped again on days 21 and 25 (each flank 2 x 2 cm) and shaved on day 21.

2.3.3 Induction phase by intradermal and cutaneous routes

2.3.3.1 Intradermal route

On day 1, 6 intradermal injections were made into a clipped area (4 x 2 cm) in the scapular region, using a needle (diameter: 0.50 x 16 mm, Terumo: C.M.L., 77140 Nemours, France) mounted on a 1 ml glass syringe (0.01 ml graduations, Record: Carrieri, 75005, Paris, France). Three injections of 0.1 ml were injected into each side of the animal, as follows:

Control group (figure 1)

. Freund's complete adjuvant diluted to 50% with an injectable isotonic solution (NaCl 0.9%),
. vehicle,
. a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution and the vehicle.

Treated group (figure 2)

. Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution,
. test substance at a concentration of 25% in the vehicle,
. a mixture of 50/50 (v/v) Freund's complete adjuvant diluted to 50% with a sterile isotonic aqueous NaCl solution, and, the test substance at a concentration of 25% in the vehicle.

2.3.3.2 Cutaneous route

On day 7, the scapular area was clipped. As the test substance is shown to be non-irritant after occlusive cutaneous treatment during preliminary test, the animals were treated with 0.5 ml of sodium laurylsulphate (10%) in vaseline to provoke local irritation.
On day 8, a cutaneous application on the 6 injection areas (4 x 2 cm) of the scapular region was performed.

Control group
. application of 0.5 ml of the vehicle.

Treated group
. application of 0.5 ml of the test substance.

The test substance and the vehicle were prepared on a compress (Semes France, 54183 Heillecourt, France), which was then applied to the scapular region and held in place for 48 hours by means of an adhesive hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).

No residual test substance was observed at removal of the dressing.
One hour after removal of the occlusive dressing, cutaneous reactions were recorded.

2.3.3.3 Challenge phase

At the end of the rest period on day 22, the test substance was applied at the Maximum Non-Irritant Concentration (M.N.I.C.) i.e. in its original form.

On day 22, the animals from both groups received an application of 0.5 ml of the M.N.I.C. of the test substance on the posterior right flank, and 0.5 ml of the vehicle on the posterior left flank. This application was performed using a 1 ml glass syringe (0.01 ml graduations, Record: Carrieri, 75005 Paris, France). The articles were prepared on a dry compress (Semes France, 54183 Heillecourt, France), then applied to the skin. The compress was held in contact with the skin for 24 hours of means by an occlusive, hypoallergic dressing (Laboratoires de Pansements et d'Hygiène, 21300 Chenove, France) and an adhesive anallergic waterproof plaster (Laboratoire des Professions Médicales, 92240 Malakoff, France).
No residual test substance was observed at removal of the dressing.

2.4. SCORING OF CUTANEOUS REACTIONS

Twenty-four and 48 hours after removal of the dressing from the challenge application site, the both flanks of the treated and control animals were observed in order to evaluate cutaneous reactions, according to the following scale:

Erythema and eschar formation

. No erythema 0
. Very slight erythema (barely perceptible) 1
. Well-defined erythema 2
. Moderate to severe erythema 3
. Severe erythema (beet redness) to slight eschar formation (injuries in depth) 4

Oedema formation

. No oedema 0
. Very slight oedema (barely perceptible) 1
. Slight oedema (visible swelling with well-defined edges) 2
. Moderate oedema (visible swelling raised more than 1 millimetre) 3
. Severe oedema (visible swelling raised more than 1 millimetre and extending beyond the area of exposure)..... 4

Any other lesions were noted.

2.5. CLINICAL EXAMINATIONS

The animals were observed twice a day during the study in order to record clinical signs and to check for mortality.

2.6. BODY WEIGHT

The animals were weighed individually on the day of allocation into the groups. on the first day of the study (day 1) and then on days 8, 15 and 25.

2.7. PATHOLOGY

2.7.1 Necropsy

On day 25, after the 48-hour observation period, the animals were sacrificed by CO_2 inhalation in excess.

2.7.2 Cutaneous samples

On day 25, a skin sample was taken from the treatment sites of the posterior left and right flanks of all surviving animals. The samples were preserved in 10% buffered formalin.

2.7.3 Microscopic examination

No histological examinations were performed.

2.8. DETERMINATION OF THE ALLERGENICITY LEVEL

The treated animals show a positive reaction if macroscopic cutaneous reactions are clearly visible (erythema and/or oedema ≥ 2) and different from those of the control animals, or, if "doubtful" macroscopic reactions are confirmed at microscopic examination as being due to the sensitization process. Sensitization reactions are characterized at microscopic examination by basal spongiosis, reactional acanthosis of the epidermis and infiltration of mononucleated cells into the dermis (1).

(1) Duprat, P. ; Delsaut. L. ; Gradiski, D. ; Lepage, M. : Investigations histo–pathologiques et cytologiques lors de la mise en évidence, chez le cobaye, d'une allergie cutanée de type retardé. Revue Méd. Vét. 127: 7, 1083-1101 (1976).

Determination of the allergenicity level

The allergenicity level of the test substance is calculated by comparing the number of animals showing positive reactions with the number of surviving treated animals at the end of the study.

% of animals showing a reaction	Allergenicity level	Classification
0 - 8	I	very weak
9 - 28	II	weak
29 - 64	III	moderate
65 - 80	IV	strong
81 - 100	V	very strong

According to the E.E.C. directive 91/325/E.E.C. published in the Journal Officiel des Communautés Européennes, when the reactions are positive in at least 30% of the treated animals, the test substance has sensitization properties and the sentence "R 43: May cause sensitization by skin contact" must be applied.

2.9. SUMMARY DIAGRAMS

Figure 1: control group

Chronology

Day -1 Clipping of the scapular region

Day 1 Intradermal injection

Day 7 Clipping + Sodium laurylsulphate

Day 8 Application covered by an occlusive dressing

Day 10 Removal of dressing and scoring after one hour

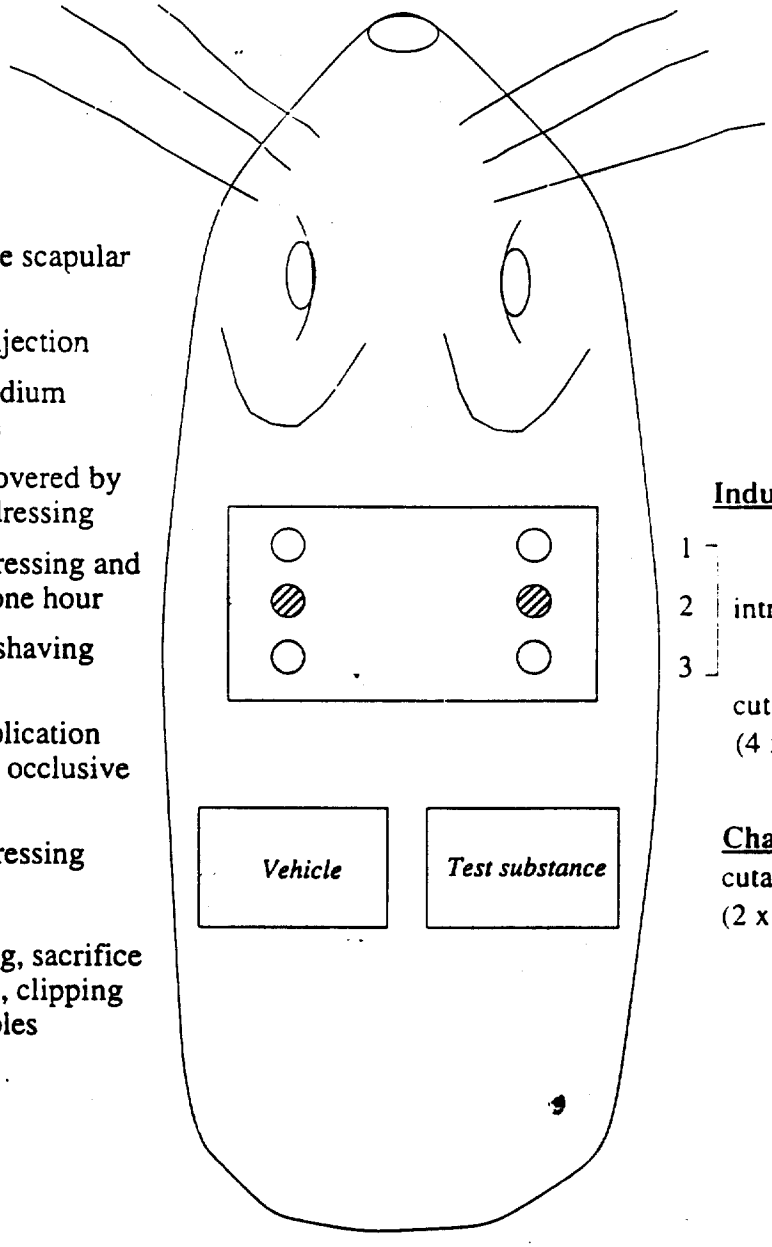
Day 21 Clipping and shaving of the flanks

Day 22 Challenge application covered by an occlusive dressing

Day 23 Removal of dressing

Day 24 First scoring

Day 25 Second scoring, sacrifice of the animals, clipping and skin samples



Induction site

1 –
2 | intradermal injections
3 –

cutaneous application (4 x 2 cm)

Challenge application

cutaneous application (2 x 2 cm)

Intradermal injections

○ 1 – 50% Freund's complete adjuvant and NaCl 0.9% solution

▨ 2 | vehicle

○ 3 – 1 + 2, 50/50 (v/v)

Figure 2: treated group

Chronology

Day -1 Clipping of the scapular region

Day 1 Intradermal injection

Day 7 Clipping + Sodium laurylsulphate

Day 8 Application covered by an occlusive dressing

Day 10 Removal of dressing and scoring after one hour

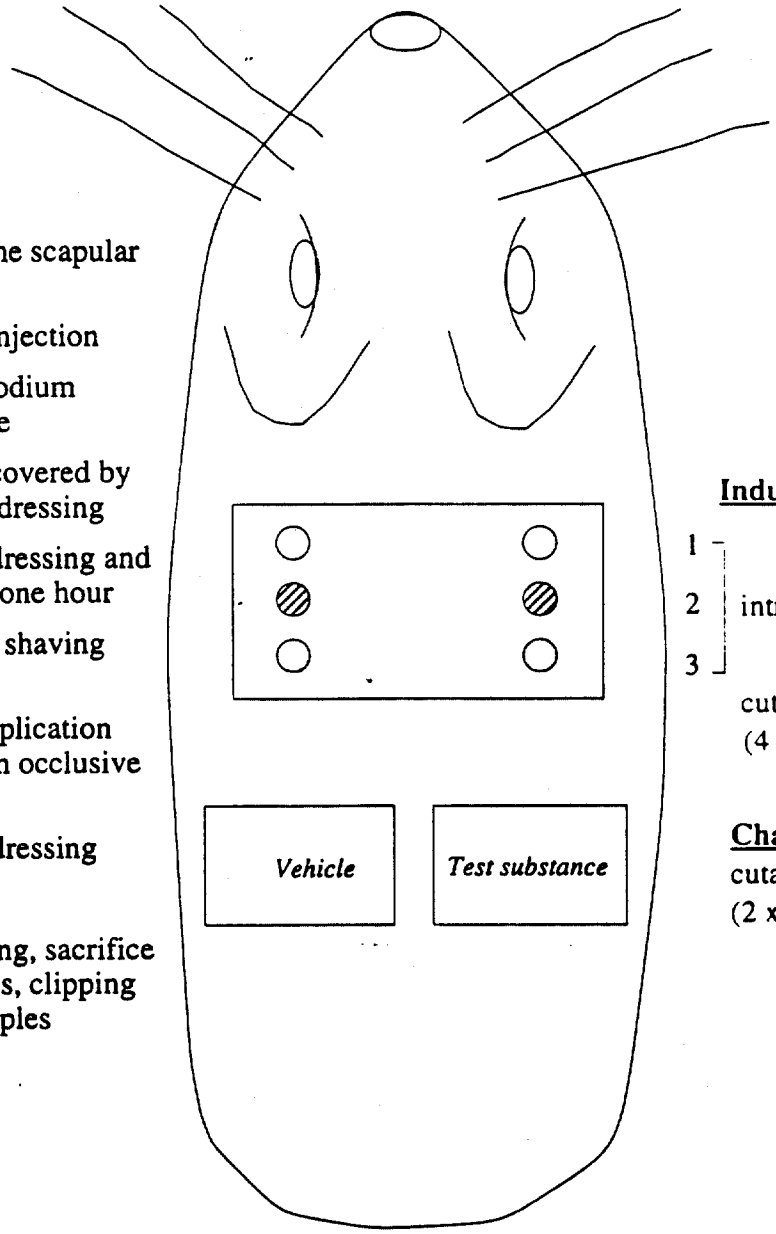
Day 21 Clipping and shaving of the flanks

Day 22 Challenge application covered by an occlusive dressing

Day 23 Removal of dressing

Day 24 First scoring

Day 25 Second scoring, sacrifice of the animals, clipping and skin samples



Induction site

1
2 intradermal injections
3

cutaneous application
(4 x 2 cm)

Challenge application

cutaneous application
(2 x 2 cm)

Intradermal injections

○ 1 50% Freund's complete adjuvant and NaCl 0.9% solution

⊘ 2 test substance and vehicle

○ 3 1 + 2, 50/50 (v/v)

2.10. CHRONOLOGY OF THE STUDY

The chronology of the study is summarized as follows:

Procedure	Date	Day
Arrival of the animals	23.9.93	-8
Allocation of the animals into groups	30.9.93	-1
Weighing, induction by intradermal injection	1.10.93	1
Laurylsulfate application	7.10.93	7
Weighing, induction by cutaneous route	8.10.93	8
Removal of occlusive dressings and scoring of local reactions after 1 hour	10.10.93	10
Weighing	15.10.93	15
Challenge cutaneous application	22.10.93	22
Removal of occlusive dressings	23.10.93	23
Scoring of cutaneous reactions after		
. 24 hours	24.10.93	24
. 48 hours	25.10.93	25
Weighing, sacrifice of the animals and skin samples	25.10.93	25

2.11. ARCHIVES

The study archives:
. protocol and possible amendments,
. raw data,
. correspondence,
. final study report and possible amendments,
. possible histological specimens:
- tissues in preservative
- blocks
- slides

are stored in the premises of C.I.T., Miserey, 27005 Evreux, France, for 5 years after the end of the *in vivo* study. At the end of this period, the study archives will be returned to the Sponsor.

3. RESULTS

3.1. PRELIMINARY STUDY

3.1.1 Administration by intradermal route

The maximal administrable concentration by intradermal route was 50% of the test substance in the vehicle in presence of Freund's complete adjuvant. Several tests were performed to determine the minimal irritant concentration which did not provoke necrosis or ulceration.

Concentration of the test substance %	Scoring after treatment 24 hours	48 hours
1	Irritation	Slight irritation
5	Irritation	Slight irritation
10	Irritation	Slight irritation
25	Irritation	Irritation
50	Necrosis	Necrosis

M.I.C. is ≥ 25%

Concentration used in the main study is 25% of the test substance.

3.1.2 Application by cutaneous route

The maximal applicable concentration by cutaneous route was 50% of the test substance in the vehicle. Several tests were performed to determine the M.I.C. and the M.N.I.C. after application of the test substance covered by an occlusive dressing for 24 hours.

Concentration of the test substance %	Scoring 24 hours after removal of the dressing (1)
1	No cutaneous reaction
10	No cutaneous reaction

M.I.C. was not determined.

(1) No residual was observed.

3.2. MAIN STUDY

3.2.1 Clinical examinations

No clinical signs or mortalities were observed during the study.

The body weight gain of the treated animals was normal when compared to that of the control animals (figures 3 and 4, appendix 3).

3.2.2 Scoring of cutaneous reactions (appendix 4)

3.2.2.1 End of the induction period

On day 10, after removal of the dressing irritation in the treated group was observed at the intra-dermal injection sites.

3.2.2.2 Challenge application

After the challenge application, a very slight (1), well-defined (2), erythema was observed at the following frequency:

Erythema

Groups	Sex	Erythema score	Scoring of the cutaneous parameters			
			24 hours		48 hours	
			LF	RF	LF	RF
Control 1	Male	0	5/5	5/5	5/5	5/5
Treated 2	Male	0	10/10	1/10	10/10	3/10
		1	-	6/10	-	6/10
		2	-	3/10	-	1/10
Control 1	Female	0	5/5	5/5	5/5	5/5
Treated 2	Female	0	10/10	-	10/10	4/10
		1	-	9/10	-	6/10
		2	-	1/10	-	-

LF: left flank (control)
RF: right flank (treated)

No oedema was observed.

After the challenge application of the test substance, no cutaneous reactions were observed in the animals of the control group.
A positive response characterised by a well-defined erythema were observed on the right flank of 4/20 and 1/20 treated animals after 24 and 48 hours, respectively. No oedema was noted. No cutaneous reactions were noted in 1 animal. Inconclusive evidence of sensitization skin reactions (very slight erythema, score of 1) were noted in 15/20 and 12/20 treated animals after 24 and 48 hours, respectively. No erythema persisted after 48 hours in 6/20 animals.

4. CONCLUSION

The test substance, CYCLOHEXYL MERCAPTAN, induced positive skin sensitization cutaneous reactions in 4/20 (20%) guinea-pigs. The allergenicity level of the test substance, CYCLOHEXYL MERCAPTAN, was WEAK (II) in guinea-pigs.

Figure 3: Male body weight gain (g)

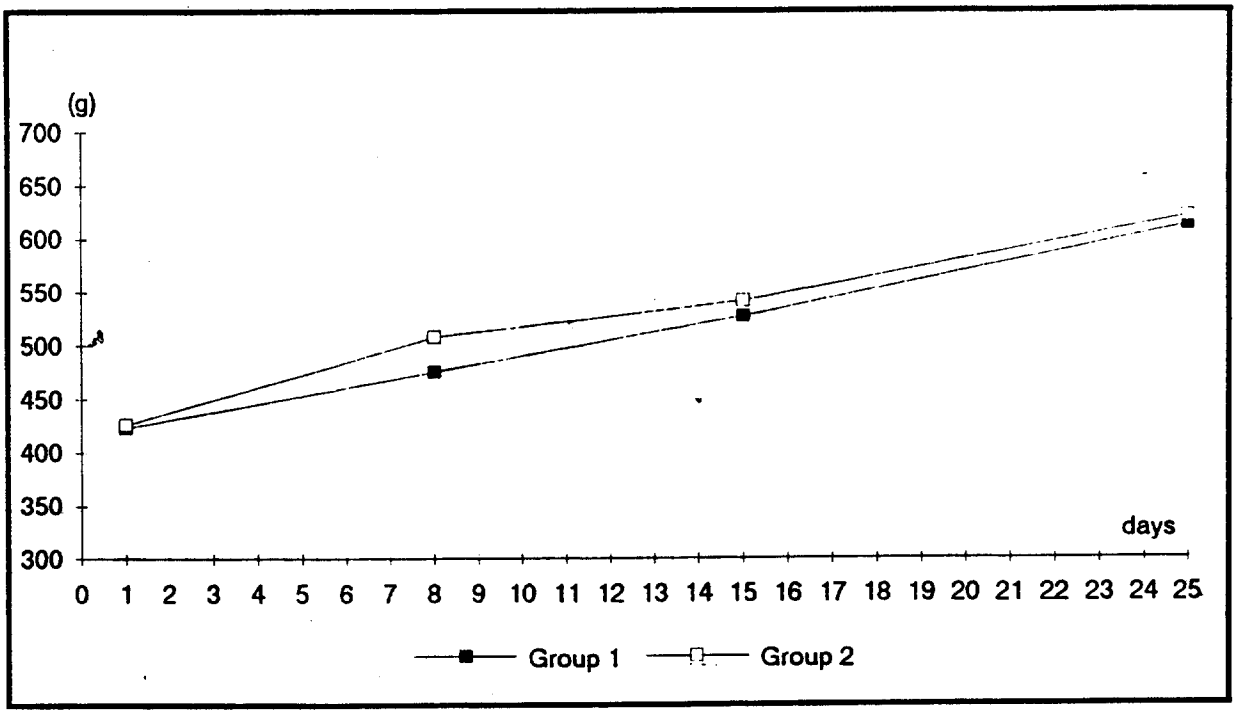
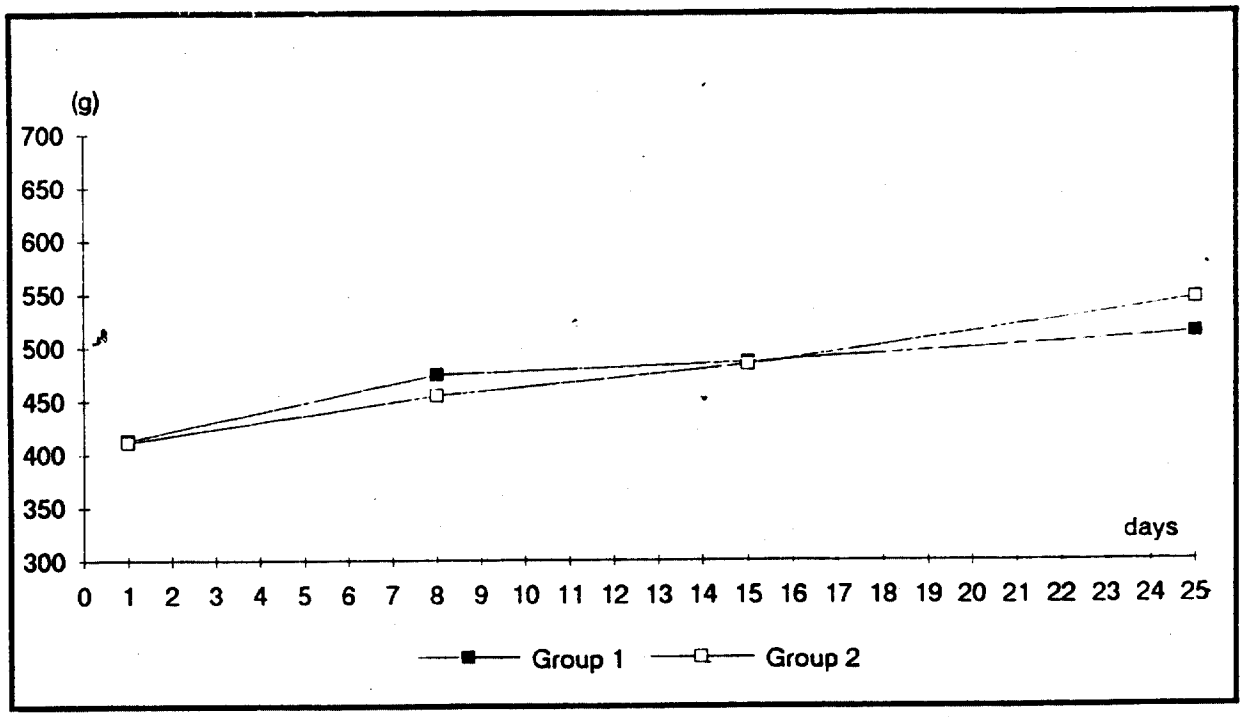


Figure 4: Female body weight gain (g)



APPENDICES

1. Test article description and certificate of analysis

TOXICOLOGY DEPARTMENT
CONFIDENTIAL
17 June 1993

elf atochem s.a.
La défense 10, cedex 42
92091 Paris-la-Défense, France

TEST ARTICLE DESCRIPTION

CYCLOHEXYL MERCAPTAN

IDENTITY

Test article name	:	Cyclohexyl mercaptan
Chemical name	:	cyclohexane thiol
CAS number	:	1569-69-3
EINECS number	:	2163787
Molecular formula	:	$C_6H_{12}S$
Molecular weight	:	116
Purity	:	99.6 % (w/w)
Origin and batch	:	Elf Aquitaine Production, Lacq, 93-6171
Elf Atochem filing number	:	CAL 3416/93

PHYSICAL AND CHEMICAL PROPERTIES

Appearance	:	colorless liquid
Viscosity	:	1.69 mPa.s at 20°C
Specific gravity	:	0.95 (20/4°C)
Melting point	:	-30°C
Boiling point	:	158-160°C at 760 mm Hg
Vapor pressure	:	5 mbar at 20°C
Flash point	:	43°C (closed cup)
Solubility	:	insoluble in water
	:	miscible with ethylic alcohol
	:	miscible with DMSO

TOXICOLOGICAL INFORMATIONS AND USE SAFETY

LD50 / Oral / Rat = 558 mg/kg. Severe eye and skin irritant.

STORAGE AND DISPOSAL

Storage	:	in dark and at room temperature
Expiry date	:	June 1994
Disposal	:	incineration

elf aquitaine production

adresse postale :
BP 22 64170 Lacq
téléphone : - 33 - 59 92 22 22
télex : pétra 560053F

direction exploration production france

ELF ATOCHEM
D.R.D.I. Dépt. de Toxicologie Industrielle
Tour Michelet
PARIS la Défense
FRANCE
A l'attention de M. REGNIER J. F.

v/réf.

n/réf. 93_6171

objet : ANALYSE du CYCLO HEXYL MERCAPTAN (CHM)

CARACTERISTIQUES		ANALYSES
Pureté	(%Pds)	99.6
Couleur	APHA	5
Pt de Trouble	C°	-71
Aspect		Liquide clair sans matière en suspension.

P.° D. Lourme

Lacq le 6 Juin 1993

M. DELOURME R.

Elf Aquitaine Production
société anonyme au capital de 1 055 000 000 F
siège social : tour Elf 2 place de la Coupole
La Défense 6 Courbevoie (Hauts-de-Seine)
rcs Nanterre B 632 022 711

2

2. Diet formula

Ref: 106

COMPLETE DIET

GUINEA-PIG MAINTENANCE DIET

Appearance: 4.5 mm diameter granules

Conditioning: bags of 25 kgs

Daily portion: water *ad libitum*, Guinea-pigs 35-50 g.

FORMULA %

Cereals	42
Grain biproducts and legumes	46
Vegetable protein (soya bean meal, yeast)	9
Vitamin and mineral mixture	3

AVERAGE ANALYSIS %

Calorific value (KCal/kg)	2600
Moisture	10
Proteins	17
Lipids	3
Carbohydrates (N.F.E.)	49
Fibre	13
Minerals (ash)	8

AMINO ACID VALUES
(calculated in mg/kg)

Arginine	8500
Cystine	2500
Lysine	7200
Methionine	2100
Tryptophan	2000
Glycine	6000

FATTY ACID VALUES
(calculated in mg/kg)

Palmitic acid	3600
Palmitoleic acid	0
Stearic acid	700
Oleic acid	5900
Linoleic acid	11200
Linolenic acid	3000

MINERALS (calculated in mg/kg)

	Nat. input	Input /MC	Total
P	7400	1400	8800
Ca	5400	5600	11000
K	12000	0	12000
Na	1300	1950	3250
Mg	3270	130	3400
Mn	60	40	100
Fe	170	150	320
Cu	10	15	25
Zn	40	45	85
Co	0.1	1.5	1.6
I	0	0	0
Cl	0	0	0

VITAMINS (calculated per kg)

	Nat. input	Synth. input	Total
Vitamin A	3500 IU	7500 IU	11000 IU
Vitamin D3	30 IU	2000 IU	2030 IU
Vitamin B1	6 mg	6.4 mg	12.4 mg
Vitamin B2	5 mg	6.4 mg	11.4 mg
Vitamin B3	22 mg	26 mg	48 mg
Vitamin B6	0.7 mg	2.7 mg	3.4 mg
Vitamin B12	0.003 mg	0.012 mg	0.015 mg
Vitamin C	0 mg	400 mg	400 mg
Vitamin E	15 mg	60 mg	75 mg
Vitamin K3	5 mg	12.6 mg	17.6 mg
Vitamin PP	97 mg	14.5 mg	111.5 mg
Folic acid	2.2 mg	1.3 mg	3.5 mg
P.A.B. acid	0 mg	2.5 mg	2.5 mg
Biotin	0.02 mg	0.06 mg	0.08 mg
Choline	1010 mg	60 mg	1070 mg
Meso-Inositol	0 mg	62.5 mg	62.5 mg

This food is supplemented with stabilized coated vitamin C, avoiding the need of other food substances (greenery, ascorbic acid) if used within 4 months of date of manufacture.

U.A.R., 7 rue Galliéni, 91360 Villemoisson - Tel: 69.04.03.57 - Fax : 69.04.81.97

3. Individual body weight values

INDIVIDUAL BODY WEIGHT VALUES
(g)

Groups	Sex	Animals	Days							
			-1	1	(1)	8	(1)	15	(1)	25
1	Male	111	433	443	-18	425	89	514	96	610
		112	394	406	82	488	60	548	63	611
		113	413	435	60	495	38	533	97	630
		114	404	408	63	471	39	510	90	600
		115	413	425	75	500	31	531	79	610
		M	411	423	52	476	51	527	85	612
		SD	14	16	40	30	24	15	14	11
	Female	126	427	430	37	467	12	479	50	529
		127	452	456	37	493	-25	468	-108	360
		128	345	365	127	492	6	498	77	575
		129	400	407	49	456	44	500	60	560
		130	406	408	57	465	20	485	58	543
		M	406	413	61	475	11	486	27	513
		SD	40	34	38	17	25	13	76	87
2	Male	116	435	444	62	506	21	527	53	580
		117	421	429	77	506	61	567	80	647
		118	389	400	109	509	22	531	94	625
		119	415	422	93	515	7	522	95	617
		120	459	466	102	568	52	620	100	720
		121	377	383	84	467	48	515	92	607
		122	399	406	69	475	41	516	82	598
		123	408	416	65	481	22	503	84	587
		124	462	462	81	543	30	573	81	654
		125	421	435	77	512	29	541	30	571
		M	419	426	82	508	33	542	79	621
		SD	28	27	16	31	17	35	22	44
	Female	131	408	417	72	489	33	522	70	592
		132	422	425	58	483	35	518	51	569
		133	439	452	-4	448	44	492	97	589
		134	368	375	69	444	40	484	52	536
		135	401	420	45	465	22	487	91	578
		136	410	413	52	465	5	470	-17	453
		137	387	392	0	392	21	413	106	519
		138	404	425	54	479	37	516	38	554
		139	406	398	41	439	41	480	69	549
		140	396	397	49	446	9	455	63	518
		M	404	411	44	455	29	484	62	546
		SD	19	22	26	28	14	33	35	42

(1) = Body weight gain
M = Mean
SD = Standard Deviation

4. Individual observation of cutaneous reactions

MACROSCOPIC EXAMINATION OF CUTANEOUS REACTIONS

Challenge application

Group	Sex	Animals	Day 24 scoring period (after 24 hours) Erythema LF	Erythema RF	Oedema LF	Oedema RF	Day 25 scoring period (after 48 hours) Erythema LF	Erythema RF	Oedema LF	Oedema RF
Control 1	Male	111	0	0	0	0	0	0	0	0
		112	0	0	0	0	0	0	0	0
		113	0	0	0	0	0	0	0	0
		114	0	0	0	0	0	0	0	0
		115	0	0	0	0	0	0	0	0
	Female	126	0	0	0	0	0	0	0	0
		127	0	0	0	0	0	0	0	0
		128	0	0	0	0	0	0	0	0
		129	0	0	0	0	0	0	0	0
		130	0	0	0	0	0	0	0	0
Treated 2	Male	116	0	0	0	0	0	0	0	0
		117	0	1	0	0	0	1	0	0
		118	0	1	0	0	0	1	0	0
		119	0	1	0	0	0	1	0	0
		120	0	1	0	0	0	1	0	0
		121	0	1	0	0	0	0	0	0
		122	0	2	0	0	0	1	0	0
		123	0	2	0	0	0	1	0	0
		124	0	1	0	0	0	0	0	0
		125	0	2	0	0	0	2	0	0
	Female	131	0	1	0	0	0	0	0	0
		132	0	1	0	0	0	1	0	0
		133	0	1	0	0	0	1	0	0
		134	0	1	0	0	0	0	0	0
		135	0	1	0	0	0	1	0	0
		136	0	2	0	0	0	1	0	0
		137	0	1	0	0	0	0	0	0
		138	0	1	0	0	0	1	0	0
		139	0	1	0	0	0	0	0	0
		140	0	1	0	0	0	1	0	0

LF: left flank (control)
RF: right flank (treated)

5. Positive control to check the sensitivity of Dunkin-Hartley guinea-pigs

Purpose: check the sensitivity of Dunkin-Hartley guinea-pigs to a positive control test article

Method	:	Magnusson and Kligman	
Test substance	:	DINITRO 2.4 CHLORCBENZENE	
C.I.T. Study - Date	:	July 1993 (CIT/Study No. 10829 TPG)	
Number of animals	:	5 females	
Induction	:	0.05% 0.5%	intradermal route day 1 cutaneous route day 8
Challenge application	:	0.1% 0.5%	right flank left flank

Conclusion

In our experimental conditions and according to the Magnusson and Kligman method, DINITRO 2.4 CHLOROBENZENE at a concentration of 0.5% induced positive skin sensitization reactions in 100% of the guinea-pigs.

INDIVIDUAL REACTIONS: CHALLENGE PHASE
MACROSCOPIC FINDINGS

Group	Sex	Animals	24-hour scoring period				48-hour scoring period				Conclusion	
			Erythema		Oedema		Erythema		Oedema			
			LF	RF	LF	RF	LF	RF	LF	RF	LF	RF
Treated	Female	16	3	2	0	0	3/S	2/S	0	0	+	+
		17	3	2	0	0	3	1/S	0	0	+	+
		18	4	2	0	0	4	2/S	0	0	+	+
		19	4	2	0	0	4	1/S	0	0	+	+
		20	3	1	0	0	3/S	0	0	0	+	+/-

+/-: bordeline
+ : hypersensitizing reaction
S : dryness of the skin
LF: left flank
RF: right flank

UNITED STATES ENVIRONMENTAL PROTECTION AGENCY
WASHINGTON, D.C. 20460

C.H. Farr, Ph.D., DABT
Manager, Product Safety and Toxicology
Elf Aftochem North America, Inc.
900 First Avenue, P.O. Box 1536
King of Prussia, Pennsylvania 19406-0018

OFFICE OF
PREVENTION, PESTICIDES AND
TOXIC SUBSTANCES

DEC 08 1994

EPA acknowledges the receipt of information submitted by your organization under Section 8(e) of the Toxic Substances Control Act (TSCA). For your reference, copies of the first page(s) of your submission(s) are enclosed and display the TSCA §8(e) Document Control Number (e.g., 8EHQ-00-0000) assigned by EPA to your submission(s). Please cite the assigned 8(e) number when submitting follow-up or supplemental information and refer to the reverse side of this page for "EPA Information Requests".

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Please address any further correspondence with the Agency related to this TSCA 8(e) submission to:

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Attn: TSCA Section 8(e) Coordinator
Office of Pollution Prevention and Toxics
U.S. Environmental Protection Agency
Washington, D.C. 20460-0001

EPA looks forward to continued cooperation with your organization in its ongoing efforts to evaluate and manage potential risks posed by chemicals to health and the environment.

Check to See if this is 12932(?) ✓ YES it IS

Sincerely,

Terry R. O'Bryan

Terry R. O'Bryan
Risk Analysis Branch

Enclosure

12931 A

12932 A

Note: I mistakenly marked and numbered 12931 twice. This one should have been labeled 12932 A. Thus, the change

Triage of 8(e) Submissions

Date sent to triage: DEC 14 1994 NON-CAP CAP

Submission number: 12932A TSCA Inventory: Y N D

Study type (circle appropriate):

Group 1 - Dick Clements (1 copy total)

ECO AQUATO

Group 2 - Ernie Falke (1 copy total)

ATOX SBTOX SEN w/NEUR

Group 3 - Elizabeth Margosches (1 copy each)

STOX CTOX EPI RTOX GTOX

STOX/ONCO CTOX/ONCO IMMUNO CYTO NEUR

Other (FATE, EXPO, MET, etc.) _____

Notes:

THIS IS THE ORIGINAL 8(e) SUBMISSION; PLEASE REFILE AFTER TRIAGE DATABASE ENTRY

For Contractor Use Only

entire document: 0 1 2 pages 1, 2 pages 1, 2

Notes: 2-sided

Contractor reviewer: POR Date: 11/1/94

CECATS\TRIAGE TRACKING DBASE ENTRY FORM

CECATS DATA:
Submission # 8EHQ- 0394 -12932 SEQ. A

TYPE: (INT) SUPP FLWP

SUBMITTER NAME: Elf Atochem North America, Inc.

INFORMATION REQUESTED: FLV P DATE:
0501 NO INFO REQUESTED
0502 INFO REQUESTED (TECH)
0503 INFO REQUESTED (VOL. ACTIONS)
0504 INFO REQUESTED (REPORTING RATIONALE)

DISPOSITION:
(0639) REFER TO CHEMICAL SCREENING
0678 CAP NOTICE

VOLUNTARY ACTIONS:
0401 NO ACTION REPORTED
0402 STUDIES PLANNED/UNDERWAY
0403 NOTIFICATION OF WORKER/CUSTOMERS
(0404) LABEL/MSDS CHANGES
0405 PROCESS/HANDLING CHANGES
0406 APP./USE DISCONTINUED
0407 PRODUCTION DISCONTINUED
0408 CONFIDENTIAL

SUB. DATE: 03/10/94 OTS DATE: 03/15/94 CSRAD DATE: 05/09/94

CHEMICAL NAME: CAS# 1569-69-3

INFORMATION TYPE:		P F C
0201	ONCO (HUMAN)	01 02 04
0202	ONCO (ANIMAL)	01 02 04
0203	CELL TRANS (IN VITRO)	01 02 04
0204	MUTA (IN VITRO)	01 02 04
0205	MUTA (IN VIVO)	01 02 04
0206	REPRO/TERATO (HUMAN)	01 02 04
0207	REPRO/TERATO (ANIMAL)	01 02 04
0208	NEURO (HUMAN)	01 02 04
0209	NEURO (ANIMAL)	01 02 04
0210	ACUTE TOX. (HUMAN)	01 02 04
0211	CHR. TOX. (HUMAN)	01 02 04
0212	ACUTE TOX. (ANIMAL)	01 02 04
0213	SUB ACUTE TOX (ANIMAL)	01 02 04
0214	SUB CHRONIC TOX (ANIMAL)	01 02 04
0215	CHRONIC TOX (ANIMAL)	01 02 04

INFORMATION TYPE:		P F C
0216	EPI/CLIN	01 02 04
0217	HUMAN EXPOS (PROD CONTAM)	01 02 04
0218	HUMAN EXPOS (ACCIDENTAL)	01 02 04
0219	HUMAN EXPOS (MONITORING)	01 02 04
0220	ECO/AQUA TOX	01 02 04
0221	ENV. OCCC/REL/FATE	01 02 04
0222	EMER INCI OF ENV CONTAM	01 02 04
0223	RESPONSE RBQEST DELAY	01 02 04
[illegible]	PROD/COMP/CHEM ID	01 02 [illegible]
0225	REPORTING RATIONALE	01 02 04
0226	CONFIDENTIAL	01 02 04
0227	ALLERG (HUMAN)	01 02 04
(0228)	ALLERG (ANIMAL)	01 02 04
0239	METAB/PHARMACO (ANIMAL)	01 02 04
0240	METAB/PHARMACO (HUMAN)	01 02 04

INFORMATION TYPE:		P F C
0241	IMMUNO (ANIMAL)	01 02 04
0242	IMMUNO (HUMAN)	01 02 04
(0243)	CHEM/PHYS PROP	01 02 04
0244	CLASTO (IN VITRO)	01 02 04
0245	CLASTO (ANIMAL)	01 02 04
0246	CLASTO (HUMAN)	01 02 04
0247	DNA DAM/REPAIR	01 02 04
0248	PROD/USE/PROC	01 02 04
0251	MSDS	01 02 04
0299	OTHER	01 02 04

TRIAGE DATA: NON-CBI INVENTORY
(YES)
NO
[illegible]

ONGOING REVIEW
YES (DROP/REFER)
NO (CONTINUE)
REFER

SPECIES
GP

TOXICOLOGICAL CONCERN:
(LOW)
MED
HIGH

USE:

PRODUCTION:

COMMENTS: Non-CAP

0 0 0 >

<ID NUMBER>

8(e)-12932A >

<TOX CONCERN>

L >

<COMMENT>

DERMAL SENSITIZATION IN GUINEA PIGS IS OF LOW CONCERN. CHALLENGE APPLICATION PRODUCED, AT 24 HOURS, WELL-DEFINED ERYTHEMA IN 20% (4/20) OF ANIMALS, AND VERY SLIGHT ERYTHEMA IN 75% (15/20) OF ANIMALS. AT 48 HOURS, 5% (1/20) HAD WELL- DEFINED ERYTHEMA, AND 60% (12/20) HAD VERY SLIGHT ERYTHEMA. EDEMA WAS NOT SEEN. $$$$
-CPSS- 0406951403